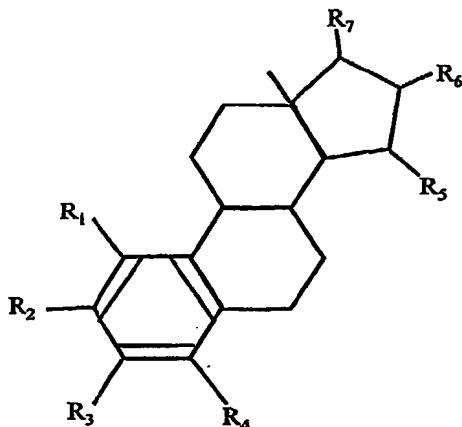


10.06.2004

## CLAIMS

(57)

1. Use of an estrogenic component selected from the group consisting of:  
substances represented by the following formula



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in which formula R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> independently are a hydrogen atom, a hydroxyl group or an alkoxy group with 1-5 carbon atoms; each of R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> is a hydroxyl group; no more than 3 of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> are hydrogen atoms;

10 precursors capable of liberating a substance according to the aforementioned formula when used in the present method, which precursors are derivatives of the estrogenic substances wherein the hydrogen atom of at least one of the hydroxyl groups has been substituted by an acyl radical of a hydrocarbon carboxylic, sulfonic acid or sulfamic acid of 1-25 carbon atoms; tetrahydrofuranyl; tetrahydropyranal; or a straight or branched chain glycosidic residue containing 1-20 glycosidic units per residue; and

15 mixtures of one or more of the aforementioned substances and/or precursors; in the manufacture of a pharmaceutical composition for use in a method of treating or preventing an immune mediated disorder in a mammal, said immune mediated disorder being selected from the group consisting of autoimmune diseases; rheumatoid arthritis; osteoarthritis; insulin dependent diabetes (type I diabetes); systemic lupus erythematosis; psoriasis; immune pathologies induced by infectious agents, viral infections or bacterial infections; tuberculosis, lepromatous leprosy; transplant rejection; graft versus host disease; atopic conditions; eosinophilia; conjunctivitis and glomerular nephritis, and said method comprising the administration of a therapeutically effective amount of the estrogenic component to said mammal.

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2. Use according to claim 1, wherein R<sub>3</sub> represents a hydroxyl group or an alkoxy group.
3. Use according to claim 1 or 2, wherein at least 3 of the groups R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> represent hydrogen atoms.
4. Use according to any one of claims 1-3, wherein the estrogenic component exhibits an 8β, 9α, 13β, 14α configuration of the steroid-skeleton, the precursors are derivatives of the estrogenic substances wherein the hydrogen atom of at least one of the hydroxyl groups has been substituted by an acyl radical of a hydrocarbon carboxylic, sulfonic acid or sulfamic acid of 1-25 carbon atoms; tetrahydrofuranyl; tetrahydropyranal; or a straight or branched chain glycosidic residue containing 1-20 glycosidic units per residue.
5. Use according to any one of claims 1-4 , wherein the method comprises the uninterrupted administration of the estrogenic component during a period of at least 5 days, preferably of at least 30 days.
6. Use according to any one of claims 1-5, wherein the method comprises oral or subcutaneous administration of the estrogenic component.
7. Use according to claim 6, wherein the method comprises oral administration.
8. Use according to any one of claims 1-7, wherein the estrogenic component is administered in an amount of at least 1 µg per kg of bodyweight per day, preferably of at least 5 µg per kg of bodyweight per day.
9. Use according to any one of claims 1-8, wherein the immune mediated disorder is a T-lymphocyte mediated disorder and/or a chronic inflammatory disease.
10. Use according to any one of claims 1-9, wherein the immune mediated disorder is selected from the group consisting of autoimmune diseases; rheumatoid arthritis; osteoarthritis; insulin dependent diabetes (type I diabetes); systemic lupus erythematosis; psoriasis; immune pathologies induced by infectious agents, viral infections or bacterial infections; tuberculosis;

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~~lepromatous leprosy; transplant rejection; graft versus host disease; atopic conditions; eosinophilia; conjunctivitis and glomerular nephritis..~~

11.10. Use according to claim 910, wherein the immune mediated disorder is a Th1 mediated disorder.

12.11. Use according to any one of claims 1-101, wherein the immune mediated disorder is selected from the group consisting of multiple sclerosis, rheumatoid arthritis, osteoarthritis, insulin dependent diabetes (type I diabetes), systemic lupus erythematosus and psoriasis.

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**13.12.** A pharmaceutical formulation comprising the estrogenic component as defined in claim 1, an immunotherapeutic agent and a pharmaceutically acceptable excipient.

14.13. The pharmaceutical formulation according to claim 123, wherein the formulation comprises at least 10 µg of the estrogenic component.

15.14. The pharmaceutical formulation according to claim 123 or 134, wherein the formulation comprises at least 1 µg of the immunotherapeutic agent.

20 16-15. The pharmaceutical formulation according to any one of claims 123-145, wherein the immunotherapeutic agent is selected from the group consisting of anti-inflammatory agents; D-pencillamine; 4-aminoquinoline agents; azathioprine; methotrexate; cyclosporin; monoclonal antibodies to T lymphocytes, adhesion molecules or to cytokines and growth factors; Tumor Necrosis Factor Receptor (TNFR)-IgG; IL-1 receptor antagonists; ICE inhibitors; betaferon; vitamin D; 1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub> and 1 $\alpha$ ,25-dihydroxyvitamin D<sub>2</sub>; agents that specifically bind a molecule selected from the group consisting of a T cell receptor, an antigen and a HLA molecule; organic gold derivatives such as gold sodium thiomalate, aurothioglucose, or auranofin; an angiogenesis inhibitor.  
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30 17.16. An oral unit dosage form comprising a pharmaceutical formulation according to any one of claims 123-156.

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